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Docket No.: 5407/1J328US1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Daryl REAL; Mike D. TOKACH; Steve S. DRITZ; Jim L. NELSEN; Robert D. GOODBAND; Jason WOODWORTH; Kevin Q. OWEN

Serial No.: 10/087,198 Art Unit: 1614

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Filed: March 1, 2002 Examiner:

For: METHOD OF ENHANCING REPRODUCTIVE PERFORMANCE IN SOWS

CLAIM FOR PRIORITY

Hon. Commissioner of
Patents and Trademarks
Washington, DC 20231

Sir:

Applicant hereby claims priority under 35 U.S.C. Section 119 based on Europe application No. 01109978.5 filed April 24, 2001.

A certified copy of the priority document is submitted herewith.

Respectfully submitted,

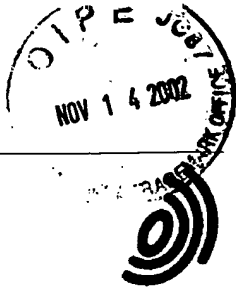
Dated: November 14, 2002

A handwritten signature in dark ink, appearing to read 'M. Collazo', is written over a horizontal line.

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Docket No. 5407/1J328US1



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Attestation

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The attached documents
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Les documents fixés à
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conformes à la version
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page suivante.

Patentanmeldung Nr. Patent application No. Demande de brevet n°

01109978.5

Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

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Blatt 2 der Bescheinigung
Sheet 2 of the certificate
Page 2 de l'attestation

Anmeldung Nr.:
Application no.:
Demande n°: 01109978.5

Anmeldetag:
Date of filing:
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Anmelder:
Applicant(s):
Demandeur(s):
Lonza AG
4052 Basel
SWITZERLAND

Bezeichnung der Erfindung:
Title of the invention:
Titre de l'invention:
Method of enhancing reproductive performance in sows

In Anspruch genommene Priorität(en) / Priority(ies) claimed / Priorité(s) revendiquée(s)

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RECEIVED
NOV 18 2002
TECH CENTER 1600/2900**Method f enhancing reproductive performance in sows**

The present invention relates to a method for improving the reproductive performance of sows.

An important factor influencing the productivity of swine operations is the rate of reproduction. Reproductive mangement includes consideration of growth and metabolism with ovarian function, and adequate energy is required to achieve full preproductive performance. It is known that dietary flushing which requires daily feed intake of sows for approximately two weeks prior to breeding may enhance ovulation rate and is believed to increase litter size.

Such an extended feeding period is costly and, depending on the Individual feed intake of every animal, does not work reliably. Also, the impact of varying the feed composition is not clearly understood.

It is an object of the present invention to avoid the disadvantages of the prior art and to provide a reliable method for enhancing the reproductive performance of sows.

This object is achieved according to the independent claims of the present invention by feeding a composition comprising carnitine and chromium.

The reproductive performance, in particular the farrowing rate, of sows is enhanced by feeding a composition comprising carnitine, an alkanoyl carnitine or salts thereof and further comprising a source of chromium, preferably chromium picolinate. Surprisingly, and in contrast to the teaching of prior art, such a combination has a synergistic effect on the reproductive performance; the farrowing rate is enhanced over at least two periods of gestation. In particular, the farrowing rate is enhanced for sows which already have passed through a first cylce of gestation, lactation and farrowing. Surprisingly, carnitine and chromium have been found to display a synergistic effect, whereas carnitine alon has no such effect on farrowing rate.

Thus carnitine and chromium increased the number of pigs born and born alive over at least two parities when comparing all sows that were started on a field test.

The carnitine according to the present invention may be carnitine, an alkanoyl-carnitine such as e.g. 3-acetyl or 3-propionyl-carnitine, or a salt thereof. The carnitine may be racemic, or preferably, may be essentially pure L-carnitine. Suitable, preferably non-hygroscopic, salts are e.g. L-carnitine tartrate, acetyl-L-carnitine tartrate, L-carnitine fumarate, L-carnitine mucate or L-carnitine-Magnesium-citrate, or any mixture of such compounds. The material may be encapsulated or otherwise protected. The carnitine may also be added to feed in the form of coated particles such as e.g. silica or starch particles or as conglomerates with e.g. edible waxes. Such particles are a further preferred embodiment.

Chromium according to the present invention is made available as chromium in the +II (divalent) or +III (trivalent) oxidation state. Preferably, the Cr is administered as a salt complex with physiologically compatible acids, such as e.g. amino acids, nicotinic acid, picolinic acid or mixtures thereof such as chromium amino niacinate or picolinate, or other forms of di- or trivalent chromium complexes such as chelates, proteinates and chromium yeast. Pure complexes of nicotinic or picolinic acid, in particular the tris-picolinate or nicotinate complexes are further preferred since they are readily resorbed in the gut of an animal. Cr-picolinate (Di- or tripicolinate) is most preferred according to the present invention since it displays the most pronounced effect if fed in conjunction with carnitine.

According to the present invention, carnitine is added to conventional diet (including drinking water) from about 20 ppm to about 1500 ppm, and preferably from about 50 ppm to about 1000 ppm. Chromium is added from about 20 ppb to about 1000 ppb, and preferably from about 50 ppb to about 800 ppb. These concentrations of either compound are the effective concentrations. The ratio between added carnitine and added chromium is not critical; the larger the amount of either one of them, the more

pronounced the synergistic effect between these compounds will be. The specific effect of such combination on reproductive performance comes as a surprise, since prior art has failed to demonstrate synergism in view of more commonly expected effects of chromium and carnitine, e.g. on lean body mass.

Preferably, dietary treatment is administered daily through the initial gestation period up to lactation and farrowing, ideally starting on the first day of breeding.

Suitable sows to be fed the diet of the present invention include but are not limited to all standard breeds of meat-producing or breeding pigs. Preferably, the sows are gestating/lactating or preferably pregnant sows, respectively. Such sows are in need of the treatment according to the present invention.

The base diet of the present invention can be any typical swine diet known in the art, including those formulated for growing, for gestating, for lactating and for finishing pigs. Extensive guidance in formulating diets for the feeding of swine can be found in 'Nutrient requirements of swine', Nutrient Requirements of Domestic Animals, Number 3, 9th rev. ed. (National Academy of Science, Washington, D. C. (1988). In the United States, for instance, most pigs are fed a diet consisting of approximately 97% corn and soybean with the remaining 3% consisting of carriers combined with one or more inorganic elements, vitamins, or antimicrobial compounds. Often, oats, vitamin and trace element premix and synthetic amino acids are added.

Example

This experiment was conducted on a commercial 1,500 sow farrow-to-wean operation in central Kansas and used 599 sows (PIC Line C22). Experimental treatments were arranged in a 2X2 factorial with main effects of added L-carnitine (0 or 50 ppm) and chromium tris-picolinate (0 or 200 ppb). Sows were started on test on the first day of breeding. Each sow remained on the same treatment through gestation, lactation, and through a second gestation period (2 parities). During gestation, all sows

were fed a grain sorghum-soybean meal-based diet formulated to contain 0.65% lysine, 0.83 % Ca, and 0.76% P. In lactation, all sows were fed a grain sorghum-soybean meal based diet formulated to contain 1.10% lysine, 0.90% Ca, and 0.80% P (Table 1). Dietary treatments were provided via a corn-based top dress fed at 30 g/d. The top dress was formulated to provide 90 mg/d and 250 mg/d carnitine in gestation and lactation, respectively. Chromium tris-picolinate was provided at 360 mcg/d and 1,000 mcg/d during gestation and lactation, respectively. These inclusions were calculated to provide 50 mg/kg carnitine (CarniFeed, Lonza Inc., NJ) and 200 mcg/kg chromium when sows were fed 4 lb/d of the gestation diet and 11 lb/d of the lactation diet. The top dress was added to the top of the feed box between meals in order to be consumed with the rest of the diet. The top dress was color coded (1% died corncobs) by treatment to assure proper distribution of experimental treatments.

At farrowing, the number of pigs born alive, as stillborn, as mummies, and total born were recorded. Total born was the sum of number of pigs born alive, stillborn, and mummies. Sows were rebred after weaning (15 d lactation) and remained on the same treatment until farrowing a second litter. If a sow did not return to estrus within 18 days, she was removed from the experiment. Sows that were bred at the start of the study, but were later found open, were removed from the trial. Procedures and data collection were identical for the second gestation and lactation period. However, dietary treatments were not administered during the second lactation period.

Calculations were made to determine the total number of pigs born, born alive, as stillborns, or as mummies per sow for the two parities. Total number of pigs were calculated using only sows that initially farrowed, then completed the second parity, as well as calculated from all the sows that were actually started on test.

Data were analyzed using the MIXED procedure of SAS. Sow was the experimental unit for the analysis with parity, previous lactation length, and/or week of farrowing as a covariate (Table 2) for total born, number of pigs born alive, mummies, and stillborn. A chi-square statistic was calculated to determine differences among treatments when analyzing percent in estrus and farrowing rate.

Results: In the first parity, a carnitine x chromium interaction ($P<0.01$) for the combination treatment was observed for first service farrowing rate (Table 2). Added dietary chromium alone improved ($P<0.01$) first service farrowing rate, but there was no added benefit from carnitine alone. However, sows fed added chromium tended to have increased ($P<0.07$) number of stillborn pigs/litter. Adding dietary carnitine improved ($P<0.05$) wean to estrus interval and tended to increase ($P<0.08$) the number of sows in estrus by d 7.

In parity 2, feeding a combination of additional dietary carnitine and chromium improved ($P<0.04$) farrowing rate of sows. There were no differences ($P>0.14$) among treatments for wean to estrus interval or percentage of sows returning to estrus by d 7 or 18.

The total number of pigs born, born alive, still born, and born mummified for both parities were calculated using *only* sows that initially farrowed (123, 140, 138, and 142, for control, added carnitine, added chromium, and both, respectively) and then completed the second parity (calculation 1). This calculation resulted in sows fed added carnitine having more ($P<0.05$) total pigs, and pigs born alive. A second calculation of sow productivity over both parities was determined using *all* sows that were started on test (148, 150, 147, and 154 per treatment, respectively). For this calculation (calculation 2), total pigs and pigs born alive were increased ($P<0.02$) for sows fed added carnitine, and(or) chromium.

Supplementing gestation and lactation diets with a combination of added carnitine and chromium had minimal effects on number of pigs born alive per litter; however, the improvement in farrowing rate observed during both parities resulted in greater overall number of pigs born over both parities. The improvement in reproductive performance from the two nutrients is synergistic.

Table 1. Common diet compositions^a

Ingredient, %	Gestation ^b	Lactation ^c
Diet		
Grain sorghum	80.18	64.10
Soybean meal (46.5%)	15.68	31.75
Other vitamin and trace mineral additions ^d	4.04	4.15
Total	100.0	100.0
Top dress^e		
Corn ^f	99.0	99.0
Corncoobs ^g	1.0	1.0

^aAll sows fed similar basal diet.

^bSows were fed 4 lb/d gestation diet; (0.7% lysine, 0.83% Ca, and 0.76% P).

^cSows were fed 11 lb/d lactation diet; (1.0% lysine, 0.90% Ca, and 0.80% P).

^dProvided 10,000,000 IU vitamin A, 1,500,000 IU vitamin D₃, 40,000 IU vitamin E, 4,000 mg menadione, 40 mg vitamin B₁₂, 9,000 mg riboflavin, 30,000 mg pantothenic acid, 50,000 mg niacin, 150 g zinc, 150 g iron, 36 g manganese, 15 g copper, 270 mg iodine, 270 mg selenium, 500,000 mg choline, 200 mg biotin, 1,500 mg folic acid, and 13,750 mg pyridoxine per ton of diet.

^eTopdress (30 g/d) was added to the top of the feed box between meals to provide carnitine and/or chromium with the rest of the feed at the next meal.

^fL-carnitine and/or chromium replaced corn to achieve dietary supplementation of 90 mg/d carnitine in gestation, 250 mg/d carnitine in lactation, 360 mcg/d chromium in gestation, and 1,000 mcg/d chromium in lactation.

^gColored corncoobs were added to distinguish treatments among one another.

Tabl 2. Eff cts of L-carnitine and chromium pic linate on reproductiv performanc ^a

Item	Treatment				Probabilities, P<			
	Control	Carnitine ^b	Chromium ^c	Both ^{bc}	SEM	Carnitine	Chromium	Int.
First parity								
No. of sows								
Started on test	148	150	147	154				
Farrowed	123	140	138	142				
First service FR ^{dei}	82.9	91.9	95.5	92.2	2.38	0.22	0.01	0.01
No. of pigs								
Total born ^e	11.3	11.4	11.5	11.6	0.30	0.62	0.57	0.90
Born alive ^e	10.0	9.8	10.2	10.2	0.25	0.32	0.63	0.71
Still born ^e	0.95	0.98	1.26	1.13	0.130	0.68	0.07	0.52
Mummies	0.34	0.26	0.39	0.34	0.060	0.26	0.29	0.77
WEI ^{dgh}	4.9	4.6	4.7	4.5	0.01	0.05	0.23	0.75
% estrus by d 7 ^{egi}	84.8	88.6	86.7	92.3	2.88	0.08	0.31	0.73
% estrus by d 18 ^{egi}	88.1	91.5	91.7	94.4	2.49	0.20	0.17	0.89
Second parity								
No. of sows								
Started	123	140	138	142				
Farrowed	87	104	102	122				
First service FR ^{degi}	70.7	73.9	74.3	85.9	3.81	0.04	0.03	0.24
No. of pigs								
Total born ^{eg}	11.1	11.2	11.0	11.4	0.37	0.50	0.94	0.81
Born alive ^{eg}	9.7	9.9	9.5	9.8	0.33	0.53	0.62	0.89
Still born ^e	1.02	1.02	1.09	1.31	0.149	0.43	0.19	0.45
Mummies	0.35	0.33	0.40	0.25	0.071	0.22	0.88	0.29
WEI ^{dgh}	4.6	4.7	4.6	4.8	0.01	0.14	0.94	0.46
% estrus by d 7 ^{efgi}	80.3	76.9	81.0	75.0	4.32	0.23	0.88	0.75
% estrus by d 18 ^{efgi}	80.2	80.8	82.9	75.9	4.17	0.40	0.77	0.32
Total pigs per sow over both parities for sows farrowed in parity 1 and completing parity 2 (calculation 1)								
Total born ^{eg}	19.4	19.8	19.5	21.3	0.59	0.04	0.15	0.25
Born alive ^{eg}	17.1	17.6	16.8	18.5	0.53	0.03	0.55	0.24

Still born ^a	1.7	1.7	2.1	2.3	0.19	0.46	0.01	0.66
Mummies	0.6	0.5	0.6	0.6	0.08	0.17	0.43	0.85

Total pigs per sow over both parities for all sows started on test (calculation 2)

Total born ^a	15.8	18.4	18.8	19.7	0.71	0.01	0.003	0.24
Born alive ^a	13.9	16.3	16.2	17.0	0.63	0.01	0.02	0.23
Still born ^a	1.4	1.6	2.0	2.1	0.17	0.35	0.002	0.94
Mummies	0.5	0.5	0.7	0.5	0.71	0.27	0.16	0.42

^aInitially 599 sows bred.

^b50 mg/kg L-carnitine provided as top dress daily.

^c200 mcg/kg chromium picolinate provided as top dress daily.

^dFR = First service farrowing rate; WEI = wean to estrus interval.

^eParity as covariate; 6.0, 5.6, 5.2, and 5.5 for control, carn., chro., and both, respectively.

^fPrevious lactation length as covariate; 15.2, 15.8, 15.7, and 15.4 for each treatment.

^gWeek of year sow farrowed as covariate; 23.6, 23.9, 23.7, and 23.9 for each treatment.

^hWEI analyzed as inverse of means, previous WEI analyzed as log of means.

ⁱP-values from chi-square statistic.

Claims

1. Method of enhancing the reproductive performance of sows wherein the sows are fed a composition comprising carnitine, alkanoyl-carnitine or a salt thereof and further comprising a source of chromium.
2. Method according to claim 1, wherein the source of chromium is chromium picolinate, preferably chromium di- or tri-picolinate.
3. Method of enhancing the farrowing rate of sows, wherein the sows are fed a composition comprising carnitine, alkanoyl-carnitine or a salt thereof and further comprising a source of chromium.
4. Use of a composition comprising carnitine, alkanoyl-carnitine or a salt thereof and further comprising a source of chromium, for enhancing the reproductive performance of sows.
5. Use of composition comprising carnitine, alkanoyl-carnitine or a salt thereof and further comprising a source of chromium, for enhancing the farrowing rate of sows.

Abstract

Feeding a composition comprising carnitine and chromlun, preferably chromium picolinate, enhances reproductive performance in sows.

24. April 2001/RGI, SREP/Lonza